

b.) Remarks

Claims 42, 44, 63 and 64 have been amended in order to recite the present invention with the specificity required by statute. Additionally, new claims 80-102 are presented in order to more specifically recite various preferred embodiments of the present invention. The subject matter of the amendment may be found in the specification as filed, e.g., at page 14, lines 5-9 and in Experiments 3 and 4 at pages 62-63. Accordingly, no new matter has been added.

Previously, Applicants discussed how, in the present invention, their fragile granules¹ are not destroyed despite the fact that lubricant is applied only on punch and die surfaces, and is not contained within the molding material. In response, the Examiner states (see page 7, lines 13-18 of the Office Action)

the features upon which applicant relies (i.e., lubricant is applied only on the die and punch surfaces) are not recited in the rejected claim(s).

Such is simply not understand at all. Prior claim 42 explicitly stated “only said die and pair of punches having said lubricant applied thereto” (lines 9-10) and “said molding material not containing any lubricant” (line 8). Each of claims 44, 63 and 64 is similar.

In that regard, all of the references upon which the Examiner relies as showing polymer-coated granules teach that such granules contain lubricant. Roche teaches that the coated granules are mixed with magnesium stearate lubricant (column 9, lines 18-21 and column 10, lines 4-7). Tuerck does the same, see column 3, lines 15-19

¹ “[D]estroyed when a molding material comprising said granule is compressed at a tableting pressure greater than 1.3 ton/cm²” (see claim 42, lines 4-5, claim 44, lines 5-6, etc.).

and column 4, lines 3-6. Accordingly, as discussed previously, the Examiner has not made out a *prima facie* case of obviousness.

Notwithstanding the foregoing, Applicants in an attempt to still further expedite prosecution have further amended the claims so as to, again address the Examiner's statements. That is, claims 42 and 63 now recite the granules' coating film is destroyed when a molding material containing them is compressed at over 1.3 ton/cm² and claims 44 and 64 recite granules comprising a base matrix that is destroyed when a molding material containing them is compressed at more than 1.3 ton/cm². Moreover, the phrase "only said die and pair of punches having said lubricant applied thereto" now reads --a die and a pair of punches in which the lubricant is applied only on surfaces of said die and said punches. Additionally, all claims still specify "said molding material *not* containing any lubricant."

As discussed below, these features are not taught by the prior art even taken collectively. Therefore, there is no *prima facie* obviousness. Moreover, Applicants' dependent claims also recite patentable subject matter in their own right. For instance, claims 99 and 100 recite the molding material is prepared "by uniformly mixing same amount of said granule with the diluting agent." Similarly, claims 101 and 102 recite use of a dry molding material.

Claims 42-53, 63-70 and 72-79 are rejected under 35 U.S.C. §103(a) as being obvious over Morimoto (EP 0 650 826), in view of Roche (U.S. Patent No. 5,075,114). These claims are also rejected as being obvious over Leal (U.S. Patent No.

3,042,531), in view of Tuerck (U.S. Patent No. 3,084,104), as well as over Tsushima (U.S. Patent No. 6,036,974), in view of Roche.

The primary references of Morimoto, Leal and Tsushima are each cited for showing tabletting machines that apply lubricant to the die surfaces. The secondary references to Roche and Tuerck are both cited as showing granules coated with polymers.

The rejections are respectfully traversed, and each is discussed in turn.

I. Morimoto in view of Roche

First, by way of background, Applicants again wish to explain that when molding material containing fragile coated granules (or granules including active substance in a base matrix) is compressed to produce a tablet, the structure of the granules is destroyed by the tabletting pressure. The present invention is specifically addressed to overcome this issue and so all claims explicitly recite the granules are damaged when compressed in a molding material over 1.3 ton/cm².

Previously, there have been two ways to address this problem and prevent destruction of these structures, namely by (i) compressing molding materials at a low tabletting pressure or (ii) adding an internal lubricant to the molding material and using a higher tabletting pressure.²

In the former case, tablets of inferior hardness are obtained and, in the latter case, there are simply some formulations in which lubricant is not desired. The inventors

² Applicants' previous statement "it is understood that even higher tabletting pressures are required when internal lubricant is omitted") at page 12, second line from the bottom of their September 27, 2005 paper should read --it is understood that higher tabletting pressure is generally permitted when internal lubricant is provided--.

of the present invention have studied these and discovered a third process that overcomes these deficiencies, namely by applying lubricant on the punches and dies of a tabletting machine so as to provide the lubricant only on the surface of the tablet.

These features are unobvious over the prior art.

Morimoto proposes a method of applying a lubricant on the punches and dies of a tabletting machine. However, Morimoto does not disclose a molding material without lubricant, e.g., not providing lubricant in the tablet.

Roche discloses a pharmaceutical tablet comprising a particle coated with polymer blend. However, Roche does not teach or suggest selecting a coating film that is destroyed when compressed at tabletting pressure greater than 1.3 ton/cm².

II. Leal in view of Tuerck

Leal does not disclose nor suggest producing a tablet by compressing molding material at or below 1.3 ton/cm².

Tuerck discloses blending powders and placing them in a coating pan (column 1, line 72 to column 2, line 3) for application of binder (column 2, lines 7-11) to form granules (column 2, lines 25-26). The granules, however, are not coated (column 2, lines 32-36), let alone being coated with a film that is destroyed when compressed at greater than 1.3 ton/cm².

In any event, Tuerck's molding materially all contain lubricant (column 3, lines 15-19, column 4, lines 28-31, column 3, lines 50-53, etc.) in contrast to the present invention.

III. Tsushima in view of Roche

Tsushima discloses an aqueous molding tablet with lubricant on its surface in order to prevent sticking during production. According to Tsushima,

10g of ubidecarenone, 300g of mannitol and 1g of sucrose fatty acid ester were mixed together, then 40ml of ethanol solution in which 2g of polyvinylpyrrolidone had been dissolved was slowly added to said mixture. A mold having a diameter of 10mm and a thickness of 5mm was filled with this mixture, then a pressure of 20Kg was exerted on the mold, the molded mixture was taken off from the mold and dried to obtain a tablet containing ubidecarenone.
(Column 8, lines 8-15.)

In Tsushima, the molding material has 10% by weight ethanol or water (column, lines 5-6) and is dried after molding.

Roche is discussed above. First, Roche does not teach or suggest a particle with a coating that is destroyed when compressed above 1.3 ton/cm². Secondly, Tsushima cannot be utilized with Roche's coated particle anyway. That is, when 10% by weight ethanol or water is added to Roche's coated granule, the structure of granule is destroyed by the ethanol or the water.

In any event, neither Tsushima nor Roche disclose applying lubricant to the punches and dies of a tableting machine, as required in all pending claims.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 42-53, 63-70 and 72-102 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



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